Remarks

Claims 18-52 are pending in the subject application. By this Amendment, Applicants have canceled claims 34 and 51 and amended claims 18, 22, 35, and 37. Support for the amendments can be found throughout the subject specification and in the claims as originally filed. Entry and consideration of the amendments presented herein is respectfully requested. Accordingly, claims 18-33, 35-50, and 52 are currently before the Examiner. Favorable consideration of the pending claims is respectfully requested.

As an initial matter, Applicants have amended the subject specification at page 1 to include a sentence indicating that the subject application is the U.S. national stage application of International patent application No. PCT/GB00/01492.

Claim 35 is objected to because of informalities. The Examiner indicates that the term "ionconductance" should be two words. Applicants gratefully acknowledge the Examiner's careful review of the claims. In accordance with the Examiner's suggestion, Applicants have replaced the word "ionconductance" with "ion conductance" in claim 35. Applicants have also changed the spelling of the word "fibre" in claims 22 and 37 to read "fiber." Accordingly, reconsideration and withdrawal of the objection is respectfully requested.

Claims 18-27, 35-39, 50, and 52 are rejected under 35 USC §102(b) as anticipated by Lewis *et al.* (U.S. Patent No. 4,917,462). In addition, claims 18-52 are rejected under 35 USC §103(a) as obvious over Lewis *et al.* (U.S. Patent No. 4,917,462) in view of Islam (U.S. Patent No. 5,485,536) and further in view of Tan (1988). The Examiner asserts that the Lewis *et al.* patent discloses a near field scanning optical microscopy (NSOM) apparatus involving a metal-coated glass pipette having a thin tip and means for determining the proximity of the aperture of the pipette to a surface. The Examiner also asserts that the Lewis *et al.* patent teaches the application of an electrical potential between the pipette and the stage, resulting in a measurable current to provide a feedback signal used to determine and control the distance between aperture and object as one of the possible means. In regard to the obviousness rejection, the Examiner asserts that it would be obvious for an ordinarily skilled artisan to use a fiber optic probe as taught by the Islam patent in an NSOM device. The Tan reference is cited as teaching that it is routine in the art to probe cells with substances that produce

visible and fluorescent light and to use a pipette probe to deliver the substances. Applicants respectfully traverse these grounds of rejection.

Applicants respectfully submit that the claimed invention is not anticipated or obvious over the Lewis *et al.* patent. The Lewis *et al.* patent refers to conventional scanning ion conductance microscopy (SICM), which utilizes non-modulated ion current to control the probe position over a sample. Independent claims 18 and 35 (and claims dependent from each) of the subject application are novel and nonobvious over the Lewis *et al.* patent, in part, because the claimed apparatus and method utilizes frequency-modulated scanning and modulation of the ion current to control the position of the probe. In the frequency-modulated mode of SICM operation, the movement of the microscope tip (ΔZ) generates modulated current (I_{MOD}). This modulated current is only generated when the probe senses the sample and is used for feedback control of the microscope. Feedback control utilizing the frequency-modulated scanning protocol has a number of additional advantages over a non-modulated mode: greater signal/noise ratio; high stability (ability to operate in a large gradient of electrolyte and with high I_{DC} drift); higher scan speed; and increase in lateral sensitivity. A further distinction of the method of use claims is that the object is imaged in a liquid environment. The Lewis *et al.* patent does not teach or suggest imaging an object in a liquid environment.

As the Examiner is aware, in order to anticipate, a single reference must disclose within the four corners of the document each and every element and limitation contained in the rejected claim. *Scripps Clinic & Research Foundation v. Genentech Inc.*, 18 USPQ2d 1001, 1010 (Fed. Cir. 1991). The Lewis *et al.* patent fails to teach or suggest an apparatus with frequency-modulated scanning and modulation of the ion current to control probe position relative to the object to be imaged. Moreover, the Lewis *et al.* patent does not teach or suggest imaging an object in a liquid environment or a means for doing so. Accordingly, the Lewis *et al.* patent does not teach or suggest Applicants' claimed invention.

In addition, Applicants respectfully assert that the claims are not obvious over the cited references, regardless of whether the references are taken alone or in combination. Applicants hereby reassert their remarks addressing the rejection under 35 USC §102 based on the Lewis *et al.* patent in regard to the rejection under 35 USC §103. The present invention possesses surprising and important advantages over the art, as indicated above. The Lewis *et al.* patent relies on non-

modulated ion current to control the probe position over a sample, whereas the subject invention utilizes frequency-modulated scanning. Moreover, Applicants respectfully assert that the apparatus of Lewis *et al.* is unsuitable for imaging living cells or samples having a convoluted surface. In contrast, the present invention can be used very satisfactorily for scanning living cells. Applicants also assert that even if Lewis *et al.* is combined with the Islam or Tan references, the claimed invention, *i.e.*, wherein frequency-modulated scanning is used, would not be achieved. It is well established in patent law that in order to support a *prima facie* case of obviousness, a person of ordinary skill in the art must find both the suggestion of the claimed invention, and a reasonable expectation of success in making that invention, solely in light of the teachings of the prior art. *In re Dow Chemical Co.*, 5 USPQ2d 1529, 1531 (Fed. Cir. 1988). One finds neither the suggestion nor the reasonable expectation of success in any of the cited references.

Applicants respectfully assert that the references cited by the Examiner under the §102 and §103 rejections do not teach or suggest, whether taken alone or in combination, Applicants' claimed invention. Accordingly, reconsideration and withdrawal of the rejections under 35 USC §§102(b) and 103(a) is respectfully requested.

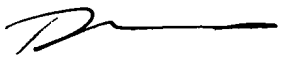
It should be understood that the amendments presented herein have been made solely to expedite prosecution of the subject application to completion and should not be construed as an indication of Applicants' agreement with or acquiescence in the Examiner's position.

In view of the foregoing remarks and amendments to the claims, Applicants believe that the currently pending claims are in condition for allowance, and such action is respectfully requested.

The Commissioner is hereby authorized to charge any fees under 37 CFR §§1.16 or 1.17 as required by this paper to Deposit Account No. 19-0065.

Applicants invite the Examiner to call the undersigned if clarification is needed on any of this response, or if the Examiner believes a telephonic interview would expedite the prosecution of the subject application to completion.

Respectfully submitted,



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